

# PATENT SPECIFICATION

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## COMPLETE SPECIFICATION

### Manufacture of Carotenoid Preparations

We, F. HOFFMANN-LA ROCHE & Co., AKTIENGESELLSCHAFT, a Swiss Company, of 124—184 Grenzacherstrasse, Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention is concerned with the manufacture of carotenoid preparations.

Carotenoids such as carotene, lycopene, bixin, zeaxanthin, cryptoxanthin, lutein, canthaxanthin,  $\beta$ -apo-8'-carotenal and esters of hydroxyl- or carboxyl-containing members of this group have attained considerable importance in technology as colouring agents. Carotenoids are yellow to red pigments which possess considerable interest as replacements for synthetic colouring agents as colouring materials for foodstuffs and animal feeds since the carotenoids are identical with or related to pigments occurring in the plant and animal kingdoms. All carotenoids are relatively high-melting substances which are insoluble in water. Moreover, they are very sensitive to oxidation. These characteristics militate against direct employment of the crystalline materials for colouration of foodstuffs or animal feeds as, in this form the materials are poorly resorbed to give poor colouring effects. The above mentioned characteristics of carotenoids are especially disadvantageous in the colouring of aqueous liquid media since, as a result of their water-insolubility, it is quite difficult to obtain a homogeneous colour effect.

It has already been attempted to make carotenoid preparations suitable for practical purposes by dissolving carotenoids in oils or fats. In consequence of the slight solubility of carotenoids therein, it has only been possible, however, to attain very low concentrations of carotenoid in oil/carotenoid preparations. By making supersaturated solutions

with the aid of heat, this disadvantage can be overcome to a certain extent. Inasmuch, however, as the heating of carotenoids results in partial decomposition and (usually) isomerization, with concomitant influence on the colour tone, this procedure also fails to satisfy all requirements. Likewise, the grinding of carotenoids affects the properties of the ultimate preparation very greatly, especially when grinding to a particle size suitable for practical purposes.

It has now been found according to the invention that a carotenoid preparation of suitable degree of subdivision can be manufactured with economy of materials by emulsifying a solution of a carotenoid, the menstruum of which predominantly consists of a volatile water-insoluble carotenoid solvent, in an aqueous solution of a swellable colloid, and removing the volatile solvent from the resulting emulsion in a manner known *per se*. Further, that a second emulsion can be manufactured from the carotenoid preparation obtained in the manner described above by using additional quantities of fresh carotenoid solution and again removing the volatile solvent. By repeatedly recycling the carotenoid preparation obtained, a considerable increase of carotenoid content in the end product can be attained. This procedure can be adapted with especial advantage to a process which involves the continuous recycling of the carotenoid-containing product.

The carotenoid preparation obtained can be used as such for colouring purposes. Advantageously, however, it is converted into small dry particles by methods known *per se* (e.g. by spraying).

The swellable colloid used in the processes of the invention is preferably gelatin, gum arabic, dextrin or polyvinyl alcohol. However, also suitable are, for example, pectin, polyvinyl-pyrrolidone, starch, methylcellulose, carboxymethyl-cellulose, gum

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tragacanth and alginates. It is advantageous to add a plasticizer to the colloid (e.g. sugar and/or sugar alcohols) in order to increase the stability of the end product toward mechanical influences. Suitable plasticizers are, for example, saccharose, invert sugar, glucose, sorbitol, mannitol and glycerine.

The menstruum of the carotenoid solutions employed in the process of the invention is preferably comprised substantially entirely of a volatile water-insoluble solvent for carotenoids, especially such solvents as are readily evaporated or steam-distilled. Appropriately employed are lower halogeno-hydrocarbons, e.g. chloroform, methylene chloride, carbon tetrachloride and trichloroethylene; the two first-named materials being especially preferred. Another good solvent for carotenoids which can be employed in the processes according to the present invention is carbon disulphide.

If the menstruum employed to dissolve the carotenoid is comprised substantially exclusively of a volatile solvent for carotenoids, there are obtained carotenoid preparations according to the invention which contain only relatively small quantities of foreign materials. In certain circumstances, however, it is appropriate to employ a carotenoid solution which contains (in addition to the volatile solvent for carotenoids) an oil or a fat, and to emulsify the resulting mixture in an aqueous solution of a swellable colloid. The volatile solvent is removed from the resulting emulsion in a manner known *per se* (e.g. by distillation, which may appropriately be carried out under diminished pressure).

A significant advantage of the process of the present invention resides in the fact that it can be carried out with significant economies in effective utilization of carotenoid starting materials. In addition, the danger of isomerization of the material is avoided, and thus the original colouring effect of the carotenoid can be maintained. The process according to the invention offers a further advantage in that it can lead to a product having an increased carotenoid content as compared to such products made by other processes.

The carotenoid preparation obtained after removal of the volatile solvent is a viscous highly-coloured sol when a non-gelable colloid is employed, but otherwise the sol solidifies with formation of a gel. The carotenoid is exceptionally finely divided in the preparation, and without difficulty preparations can be obtained in which the bulk of the carotenoid is present in a degree of fineness of from about 2 to 3 microns, particles above 5 microns in size being substantially absent. The product, even when in gel form, can also be diluted with water in desired proportions and the carotenoid pigment is uniformly dispersed in the solution and is stable

in this condition. When a dry powder is made by spraying the foregoing sols, the powder can likewise be dissolved in water with the attainment of a uniform dispersion.

The following examples are illustrative of the process of the invention:—

#### EXAMPLE 1

1500 g of gelatin are dissolved in 1.5 l. of water, mixed with a solution of 300 g of saccharose in 300 ml of water and the whole heated to 50° C. Then, a solution of 210 g of *trans* betacarotene in 800 ml of acid-free chloroform, at 50° C., is added to the mixture, while emulsifying mechanically and with precautions to exclude atmospheric oxygen. The resulting emulsion is then freed of chloroform by distillation at 50° C. under reduced pressure, whereby approximately 3800 g of a suspension of uniformly fine solid betacarotene particles (1 to 3 microns) are formed. Upon cooling, the sol goes over to a gel. The latter contains about 5% *trans* betacarotene. It can be diluted with water upon slight heating, or can be sprayed and worked up to a dry powder.

#### EXAMPLE 2

1500 g of gum arabic are dissolved in 1.5 l. of water and mixed with a solution of 300 g of invert sugar in 300 ml of water. This solution is heated to 35° C. and is continuously fed into an emulsifying apparatus, simultaneously with a solution of 450 g of *trans*- $\beta$ -apo-8'-carotenal in 3.2 l. of methylene chloride at 35° C. The emulsion produced is continuously drawn off into a distillation apparatus and there freed of methylene chloride at 50° C. under reduced pressure. There is thus obtained about 4 kg of a sol or gel containing about 10% of uniformly fine *trans*  $\beta$ -apo-8'-carotenal (1 to 3 microns).

#### EXAMPLE 3

1500 g of gelatin are dissolved in 1.5 l. of water, mixed with a solution of 300 g of sorbitol in 900 ml of water and heated to 50° C. Into this mixture is introduced, slowly and while emulsifying mechanically, a solution of 1800 g of *trans*  $\beta$ -apo-8'-carotenic acid methyl ester in 4 l. of carbon tetrachloride at 50° C. During the emulsification procedure, a portion of the emulsion is continuously removed through a suction tube and introduced into a distillation apparatus where it is freed of carbon tetrachloride by distillation at 50° C. under reduced pressure and the product obtained recycled to the emulsification vessel. Thus the proportion of finely divided carotenoid in the emulsion is gradually increased, without destruction of the emulsion by reason of excessive content in the organic phase. The sol or gel produced (about 5.4 kg) contains at the end of the pro-

cedure about 30% of *trans*  $\beta$ -apo-8'-carotenic acid methyl ester in homogeneous, finely divided form (1 to 3 microns).

#### EXAMPLE 4

5 1800 g of dextrin are dissolved in 1.8 l. of water. This solution is heated to 40° C. and, simultaneously with a solution of 475 g of *trans* canthaxanthin in 2 l. of carbon disulphide at 40° C., is continuously introduced into an emulsifying apparatus. The emulsion produced is continuously transferred to a distillation apparatus, and there freed of carbon disulphide at 50° C. under reduced pressure. In the suspension thus produced, 15 which contains about 10% of canthaxanthin, is emulsified in a second step, by repeating the process, a solution of an additional quantity of 475 g of canthaxanthin in 2 l. of carbon disulphide. After again continuously 20 freeing the mixture of solvent, there is obtained about 4.5 kg of a sol or gel having a content of about 20% *trans* canthaxanthin.

#### EXAMPLE 5

25 1000 g of polyvinyl alcohol are dissolved in 2 l. of water and mixed with a solution of 300 g of glycerine in 300 ml of water. The solution is heated to 50° C. and is introduced continuously, simultaneously with a solution of 530 g of *trans*  $\beta$ -apo-8'-carotenal in 1.8 l. of trichloro-ethylene at 50° C., into an emulsifying apparatus. The emulsion formed is continuously introduced into a distillation apparatus, there freed of trichloro-ethylene at 50° C. under reduced pressure, and immediately introduced into a second emulsifying apparatus, together with a fresh solution of 530 g of *trans*  $\beta$ -apo-8'-carotenal in 1.8 l. of trichloro-ethylene at 50° C. In a second distillation apparatus, the trichloro-ethylene is again removed. The entire procedure is again carried out in a third emulsifying and third distillation apparatus in a similar manner, so that a total of 1590 g of *trans*  $\beta$ -apo-8'-carotenal is processed in three stages. There is thus obtained about 5 kg of a sol or gel having a content of about 30% *trans*  $\beta$ -apo-8'-carotenal. 45

#### EXAMPLE 6

50 300 g of gelatine are dissolved in 300 ml of water, mixed with a solution of 1500 g of saccharose in 1500 ml of water, and heated to 50° C. By treating the solution formed

with 210 g of *trans* betacarotene according to the method described in Example 1, there is obtained a product that is easily soluble in cold water. 55

#### WHAT WE CLAIM IS:—

1. A process for the manufacture of a carotenoid preparation containing the carotenoid in finely divided form, which process comprises emulsifying a solution of a carotenoid, the menstruum of which predominantly consists of a volatile water-insoluble carotenoid solvent, in an aqueous solution of a swellable colloid, and removing the volatile solvent from the resulting emulsion in a manner known *per se*. 60

2. A process in accordance with Claim 1, wherein the product is recycled until the desired carotenoid content in the final carotenoid-preparation is obtained. 65

3. A process in accordance with Claim 1 or Claim 2, wherein the carotenoid-containing product obtained after the elimination of the volatile solvent, or after the final elimination of the volatile solvent in the case where recycling is adopted, is transformed into dry particles in a manner known *per se*. 70

4. A process in accordance with Claim 3, wherein said dry particles are formed by spray drying technique. 75

5. A process in accordance with any one of the preceding claims, wherein a plasticiser is added to the aqueous solution of swellable colloid. 80

6. A process in accordance with any one of the preceding claims, wherein said volatile water-insoluble solvent for carotenoids is a lower halogeno-hydrocarbon such as chloroform or methylene chloride. 85

7. A process in accordance with any one of the preceding claims, wherein the swellable colloid used is gelatin, gum arabic, dextrin or polyvinyl alcohol. 90

8. A process for the manufacture of carotenoid preparations containing the carotenoid in finely divided form, substantially as described with reference to the examples given. 95

9. Carotenoid preparations containing the carotenoid in finely divided form, when manufactured by the process claimed in any one of the preceding claims. 100

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